of two-dimensional echocardiographic wall-motion analysis at baseline and during increments of intravenous dobutamine infusion. If an adequate chronotropic response (heart rate ≥ 85% of predicted maximum) is not achieved, small aliquots of atropine sulfate are administered intravenously to augment the heart rate further. Heart rate, echocardiographic images, blood pressure, and an ECG are recorded at the end of each stage. Myocardial ischemia is detected if substantial ST segment changes develop or a regional wall-motion abnormality is seen on two-dimensional echocardiography. Interpretation of stress echocardiography studies has been further enhanced by digital technology, which displays the images side by side for easy comparison. Diagnostic studies can be obtained in most patients, but may be limited by inadequate images or adverse side effects.

The specificity and sensitivity of detecting the presence of coronary artery disease by dobutamine stress echocardiography are comparable to exercise-stress nuclear studies when done by experienced laboratory technicians. The overall sensitivity and specificity of detecting coronary artery disease in patients with normal resting regional wall motion are 87% and 91%, respectively. The sensitivity increases to 97% in patients with multiple vessel disease. By localizing the region of inducible myocardial abnormalities, two-dimensional echocardiography can also identify a stenosed major coronary artery.

Dobutamine stress echocardiography has been used in evaluating patients after myocardial infarction for the detection of residual viable myocardium. Immediately after a prolonged ischemic insult, it is important to distinguish between necrotic and stunned but viable myocardium. This question becomes important clinically in determining the need for revascularization procedures. Low-dose dobutamine (5 to 10 μg per kg per minute) improves regional myocardial function in the area of viable myocardium but not in an area of myocardial necrosis.

The noninvasive detection of multivessel coronary artery disease and residual jeopardized myocardium is essential after myocardial infarction. If the patient has multivessel disease, dobutamine stress echocardiography will show a regional wall-motion abnormality in an area remote to the primary infarct site. Substantial residual stenosis in an infarct-related artery results in worsening of the preexisting regional myocardial abnormality. In addition, patients with an abnormal dobutamine stress echocardiogram after myocardial infarction have a higher incidence of future cardiac events compared with those who had a normal study.

Dobutamine stress echocardiography can be used to stratify the degree of risk in patients who are referred for a noncardiac vascular surgical procedure. The absence of an inducible new wall-motion abnormality with dobutamine stress echocardiography is an excellent negative predictor for postoperative cardiac events. A positive test, however, does not necessarily predict the development of postoperative cardiac complications.

The safety of dobutamine stress echocardiography has been shown in a large series of patients. Noncardiac side effects are usually minor and include nausea, anxiety, headache, and tremor. Cardiac side effects such as angina and supraventricular and ventricular arrhythmias do occur, but are usually well-tolerated and rarely require treatment. In more than 1,000 patients who have had dobutamine stress echocardiography, serious complications from myocardial ischemia did not occur. Symptomatic ischemia or arrhythmias were effectively treated with test termination, sublingual nitroglycerin, or short-acting β-blocker drugs.

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Tuberculosis and Human Immunodeficiency Virus Disease

THE ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS) epidemic has exposed persons with the human immunodeficiency virus (HIV) and those who care for them to new dangers from an old pathogen, tuberculosis. Individual and public health risk can be reduced by conscientious adherence to reasonable exposure precautions, early screening, and informed selection of antituberculous regimens to treat both exposure and active disease.

It is estimated that 3 million people worldwide are infected with both Mycobacterium tuberculosis and HIV. In the United States, 5% to 10% of the 1 million persons infected with HIV are also infected with M tuberculosis. This rate is probably higher in areas with large homeless, injection drug using, or immigrant groups. The increasing incidence of tuberculosis (TB) in the United States since 1984 is generally attributed to cases associated with the AIDS epidemic. Further, in recent outbreaks on the East Coast, 96% of cases of multidrug-resistant TB occurred in HIV-infected persons. Unlike most opportunistic pathogens, M tuberculosis is contagious and causes potentially serious illness in immunocompetent as well as immunocompromised hosts.

Nosocomial transmission of tuberculosis to both staff and patients has been well documented. Of particular concern is the transmission of TB or multidrug-resistant TB (infection with M tuberculosis resistant to both isoniazid and rifampin) to patients and health care workers with HIV. Tuberculosis in HIV-infected hosts rapidly progresses, disseminating to extrapulmonary sites in as many as 70% of patients. DNA analysis of M tuberculosis organisms has shown that primary TB developed within five months of exposure in 37% of HIV-infected persons exposed to a source patient, compared with the 2% to 4% of immunocompetent contacts in whom TB develops within a year of exposure. Of patients with advanced HIV dis-

ease who are infected with *M tuberculosis* by such exposure, progression to active disease is expected in virtually all patients in the absence of prophylaxis.

Multidrug-resistant TB in non-HIV-infected patients is associated with high mortality, long hospital stays, and frequently failure of even the best available treatments. Patients with multidrug-resistant TB may remain infectious for several months after treatment is initiated, and the risk to staff is increased accordingly. In HIV-infected patients, multidrug-resistant TB can be devastating, with death occurring a median of one to four months after diagnosis. Multidrug-resistant strains usually develop through selection during the treatment of TB. In HIV infection, however, multidrug-resistant TB has also been shown to result from infection with exogenous drug-resistant strains of *M tuberculosis*, which can occur even during therapy for drug-susceptible TB. These recent data, and the guarded prospects for new therapies for either HIV infection or TB in the near future, show the importance of preventing exposure to TB, aggressive screening, and secondary prophylaxis of exposed persons.

Patients at high risk for tuberculosis—including injection drug users, homeless persons, incarcerated persons, immigrants from TB-endemic areas, and contacts of persons with infectious TB—presenting with cough or other respiratory symptoms should be placed on respiratory precautions until TB is excluded by three sputum specimens negative for *M tuberculosis* on acid-fast bacilli staining or another diagnosis is established that fully explains the patient's presentation. Even in the latter situation, it is prudent to document at least one negative sputum smear on acid-fast bacilli staining. In the hospital, respiratory precautions include private, negative-pressure rooms with at least six room-air changes per hour and no recirculation of air into the rest of the building. Masks to filter out 1-μm particulates should be worn by all staff and visitors entering the room to prevent inhalation of aerosolized mycobacteria. The room door should remain closed; patients leaving their room should wear a mask. Patients with smears positive for acid-fast bacilli should remain on respiratory precautions until they have received adequate therapy for at least two weeks, show clinical improvement, and show a decrease in acid-fast bacilli on quantitative sputum smears.

Screening and secondary prophylaxis are crucial in the care of persons with HIV. The rate at which active tuberculosis develops in HIV-infected persons with positive skin tests is 10% per year in the absence of prophylaxis, compared with a 10% total lifetime risk in HIV-negative adults who have positive purified protein-derivative (PPD) skin tests. The prevalence of anergy increases with the progression of HIV infection: only 10% of HIV-positive patients with T-helper (CD4+) cell counts of 200 to 400 cells × 10⁶ per liter (200 to 400 per mm³) are anergic, compared with two thirds of those with CD4+ counts of less than 200 × 10⁶ per liter. Purified protein-derivative skin testing with two controls should be done as early as possible in patients at risk for HIV infection and, if negative, should be repeated every 6 to 12 months until anergy supervenes.

Because of the likelihood of a reduced cutaneous immune response and the serious consequences of a false-negative result, a positive PPD test is defined as 5 mm or more of induration, in contrast to the 10-mm cutoff used in non-HIV-infected people. Anergy is defined as 2 mm of induration or less in response to all three antigens. Persons with positive PPD tests are treated for one year with a regimen of isoniazid, in contrast to the six-month regimen used in HIV-negative patients. Studies are under way to assess the effectiveness of shorter courses. Chemoprophylaxis results in a severalfold reduction in the incidence of progression to active disease and is administered to HIV-positive patients regardless of age or length of time since PPD conversion. Chemoprophylaxis of anergic patients with HIV is also recommended when a patient is at high risk for TB by social factors, has a history of untreated positive PPD tests at any time in the past, or has been in close contact with an infectious patient with TB. Patients infected with HIV who are exposed to multidrug-resistant TB should receive prophylaxis with at least two drugs to which the presumed source strain is shown to be susceptible. In these patients, the Centers for Disease Control and Prevention recommends a regimen that includes pyrazinamide and ethambutol hydrochloride or pyrazinamide and a fluoroquinolone (ciprofloxacin or ofloxacin).

Human immunodeficiency virus-infected patients with active tuberculosis that is not drug-resistant generally respond well to therapy. Because of the increasing prevalence of multidrug-resistant TB, initial therapy with four drugs—isoniazid, 300 mg; rifampin, 600 mg; pyrazinamide, 25 mg per kg; and ethambutol, 15 mg per kg—is recommended for all patients, immunocompromised or not. Appropriate modifications are then made as sensitivities become available from sputum cultures. If exposure to a multidrug-resistant strain is suspected, if the patient has been previously treated for TB, or if positive sputum cultures persist after three months of compliance with treatment, a specialist should be consulted. In general, a regimen for multidrug-resistant TB should contain at least three drugs to which the organism is susceptible and may involve 18 months or more of treatment.

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Hormonal Therapy for Metastatic Prostate Cancer

THE MEDIAN TIME from the diagnosis of metastatic prostate cancer to death is 2.5 years. The vast majority of the 34,000 deaths per year from prostate cancer in the